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The Brief Case: Incidental Finding of Cystic Echinococcosis during Evaluation for Hepatitis

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KEYWORD *Echinococcus*

CASE

A 16-year-old who immigrated from Kenya was referred to the gastroenterology service 6 months postpartum for evaluation of hepatitis B virus infection discovered during routine prenatal screening. The patient had no abdominal pain, nausea, vomiting, diarrhea, or decreased appetite. An ultrasound of the liver was performed and demonstrated a multilocular cystic mass. Magnetic resonance imaging (MRI) of the abdomen revealed a large multiloculated cystic lesion measuring 10.5 by 7.7 by 7.6 cm centered in the left lobe of the liver and containing numerous smaller cysts. Given the patient's age and history of living in Kenya, the lesion was most consistent with hepatic echinococcosis, but mesenchymal hamartoma, hepatic pyogenic abscess, and biliary cystadenocarcinoma were included in the differential diagnosis. The patient was treated with albendazole for 6 weeks. Given the complex nature of the hepatic cyst, percutaneous drainage (consisting of puncture, aspiration, injection, and reaspiration [PAIR]) of the hepatic cyst was not an option. Therefore, the patient underwent an abdominal exploratory laparotomy and excision of the cyst. All daughter cysts as well as the gelatinous cyst lining were removed intact without any spillage of contents. The cyst cavity was irrigated multiple times with 23.4% hypertonic saline, a scolicidal agent. Two specimens were received in the pathology lab. The first, labeled "main cyst wall," consisted of fibrous connective tissue. The second specimen, labeled "daughter cysts," consisted of multiple intact yellow cysts of various sizes ranging from 0.6 to 10.4 cm (Fig. 1). Small cysts within larger cysts were identified. Some of the cysts contained clear fluid, while others contained yellow amorphous material. Microscopically, the sediment or "hydatid sand" within the fluid of the cysts showed many shed hooklets, with a characteristic scimitar shape, and small calcareous bodies. The hooklets were birefringent under polarized light. The cyst lining was composed of two layers consisting of a pathognomonic 1-mm-thick, acellular laminated membrane as well as a thin, translucent, nucleated germinal membrane. Ovoid 100-μm invaginated protoscolices containing two rows of hooklets and suckers were seen budding from the germinal membrane (Fig. 2).

The patient was discharged after cyst removal with a 2-week regimen of albendazole and recovered well with no complications. A 6-month follow-up ultrasound showed no active infection in the area of the previous surgery site. The patient was lost to further follow-up and did not return for her postsurgery MRI.

DISCUSSION

Echinococcosis is infection with cestodes of the genus *Echinococcus* (1). Their life cycle involves two mammalian hosts, typically a carnivore definitive host and an herbivore intermediate host (2, 3). Humans may become an accidental intermediate host, resulting in three forms of disease: cystic, alveolar, and polycystic, caused by *Echinococcus granulosus sensu lato*, *Echinococcus multilocularis*, and *Echinococcus vogeli*,

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For answers to the self-assessment questions and take-home points, see https://doi.org/10.1128/JCM.01571-18 in this issue.

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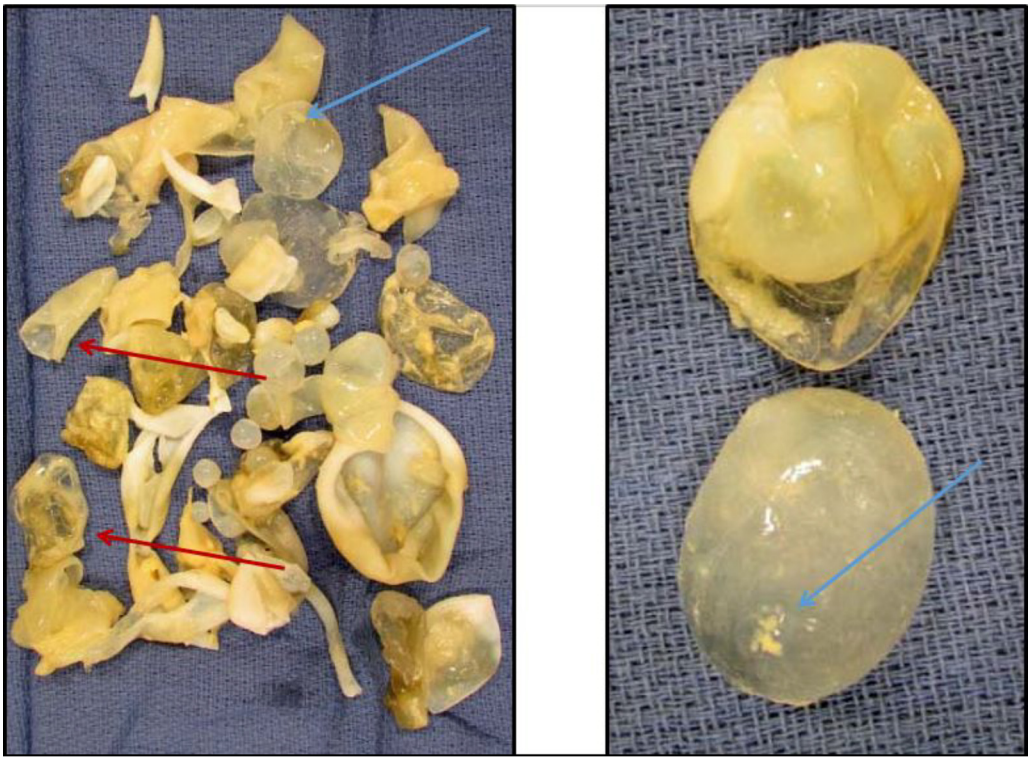

FIG 1 Gross appearance of yellow tan cysts and daughter cysts filled with clear fluid and hydatid sand. Fragmented cyst walls that are curled and deflated (red arrows) intermixed with intact small daughter cysts are shown. Pictures courtesy of Connie Thorpe.

respectively. The intermediate hosts, geographic distributions, and organ locations are different for each form (1).

Cystic echinococcosis (CE), otherwise known as hydatid disease, is the most prevalent form of the disease, with a worldwide distribution caused by *E. granulosus sensu lato*. This is a genetically diverse group with evolving taxonomy and with species-level assignments in some cases unresolved. Currently recognized species and genotypes include *Echinococcus granulosus sensu stricto* (genotypes G1 to G3), *Echinococcus*

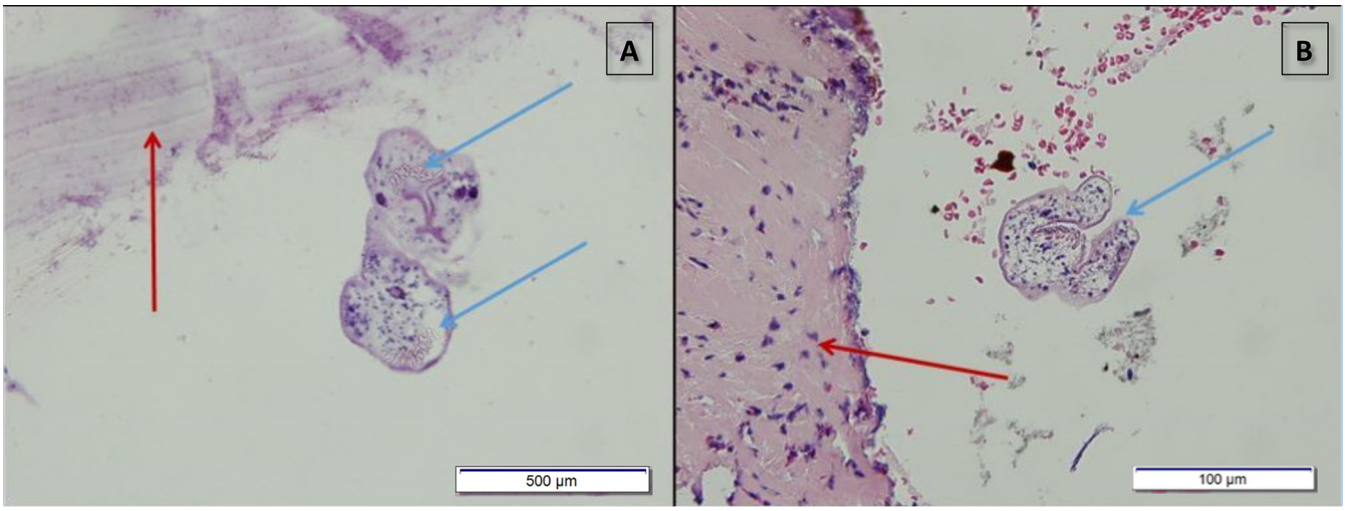

FIG 2 (A) Two scolices side by side, with refractile hooklets (blue arrow) adjacent to the outer acellular laminated membrane (red arrow) pathognomonic for this entity. (B) Hematoxylin and eosin stain of fluid from the cyst, revealing an invaginated protoscolex (blue arrow) adjacent to a portion of the "false capsule," suggesting cyst leakage and host inflammatory response (red arrow).

equinus (G4), *Echinococcus ortleppi* (G5), *Echinococcus intermedius* (G6 and G7), *Echinococcus canadensis* (G8 and G10), and *Echinococcus felidis* (2, 4, 5). These various species/genotypes display differences in host range, life cycle, and pathogenicity, with *E. granulosus sensu stricto* accounting for 88% of infections worldwide (6).

The adult tapeworm is small (2 to 6 mm in length) and consists of a scolex, with four sucking disks and a double row of hooklets by which it attaches to the small intestine of the definitive host, and three proglottids. The eggs, which are identical in appearance to those of *Taenia* species, are released from the terminal gravid proglottid, and thousands are shed in the feces of an infected definitive host each day. These eggs may be ingested by one of a number of mammalian intermediate hosts, mostly ungulates (sheep, goats, pigs, horses, etc.), which harbor the larval stage. As mentioned above, humans act as an accidental intermediate host and do not play a role in the natural life cycle. The eggs may be ingested with contaminated food or water, by fomites, or by direct contact with infectious dogs. Once the ingested eggs hatch, they release oncospheres that penetrate the intestinal mucosa of the intermediate host and are carried by the circulatory system to lodge in the organs, with the most common sites being the liver, followed by the lungs and, to a lesser extent, the brain, heart, bone, and other tissues. Within the tissues, the oncosphere gradually expands and forms hydatid cysts characterized by an acellular, laminated outer layer and a cellular, germinal inner membrane from which daughter cysts or brood capsules arise, each having the potential of developing multiple invaginated protoscolices. The definitive host becomes infected by ingesting the cyst-containing organs of the infected intermediate host. After ingestion, the protoscolices exvaginate, attach to the intestinal mucosa, and develop into adult stages which lay eggs and repeat the cycle (7). Since humans are an accidental intermediate host, they do not harbor the adult form of the tapeworm in their intestines and do not shed eggs in their stools. This is an important clinical point since a stool oocyte and parasite test would not be diagnostic.

Infected humans may remain asymptomatic for years and the diagnosis may be incidental, such as in our case. The rate of cyst growth is variable, and compression of the cyst on internal organs or rupture of the cyst contents leads to symptoms including right upper quadrant abdominal pain, hepatitis, cholangitis, and anaphylaxis due to leakage of the cyst contents (8). The cysts grow about 1 mm a month, but clinical features usually do not appear until the cysts reach about 10 cm in diameter (8), although smaller cysts can impinge on important structures, or those that have ruptured may also cause symptoms. Pregnancy can be a particularly vulnerable state when cysts can potentially rupture even at smaller sizes due to the compressive effects of the gravid uterus on the liver as well other abdominal organs. Rupture of these thin-walled cysts can lead to anaphylactic shock or sudden death for both mother and baby (9). Fortunately, in our patient's case, even though the cyst was over 10.0 cm, pregnancy did not complicate her disease and she remained asymptomatic until infection was incidentally discovered.

The diagnosis of cystic echinococcosis relies on imaging supported by serology. The World Health Organization Information Working Group on Echinoccoccosis (WHO-IWGE) categorized the disease based on ultrasonagraphic findings. The classification allocates the cysts into three relevant groups—active, transitional, and inactive—and is used for staging of the disease as well as treatment decisions. Computed tomography and magnetic resonance imaging are also used in cases in which the cysts cannot be accessed through ultrasound.

The WHO-IWGE case definition for probable or confirmed cases of cystic echinococcosis includes the demonstration of serum antibodies by two separate serological assays; a high-sensitivity test followed by a high-specificity test (10). Serological testing options for cystic echincococcosis include indirect hemagglutination (IHA), indirect fluorescent antibody (IFA), enzyme-linked immunosorbent assay (ELISA), and latex agglutination, assays which detect antibody to crude or purified hydatid cyst fluid antigens. The sensitivity of this testing has been reported as 85 to 98% for cysts located in the liver, with significantly lower sensitivity for lung infection (10). Sensitivity is also affected by factors such as cyst maturity and cyst wall integrity (5). Significant cross-

reactivity is seen with other parasitic conditions, including cysticercosis, as well as other nonparasitic conditions, including malignancy and cirrhosis. The CDC recommends confirmatory testing by immunodiffusion to detect antibody to echinococcal antigen 5 (Arc5) or immunoblot testing for 8-kDa and 21-kDa bands, the latter of which is offered through the CDC reference laboratory (7).

Percutaneous fine-needle aspiration biopsy under ultrasound guidance can be performed and is used in suspected cases with equivocal radiological and serological test results. Fluid can be examined microscopically to confirm diagnosis of *Echinococcus* spp. by showing hydatid sand containing free hooklets, protoscolices, deteriorating brood capsules, and calcareous corpuscles. Calcareous corpuscles are mineralized concretions found in larval cestodes and develop from an organic matrix-mediated process. They appear as granular concentric layers and vary in size and shape between different cestode species. The calcareous corpuscles are found in the protoscolex stage of *E. granulosus*; they are irregularly spherical or ovoid and range between 2 to 16 μm and may serve to provide autophagic activity (11, 12).

Treatment options for cystic echinococcus include surgery, percutaneous drainage, and medical pharmacotherapy as well as monitoring. Puncture, aspiration, injection, and reaspiration (PAIR) is a treatment option for active unilocular, simple cysts as well as transitional unilocular cysts with daughter cysts that are greater than 5 cm (13). This involves percutaneous draining of echinoccocal cysts located in the abdomen using a fine needle or catheter, followed by introduction of a protoscolicidal agent, such as alcohol or hypertonic saline, to kill any remaining parasites in the cyst cavity (10, 13). Surgery is reserved for more complicated cysts, such as in our case, that are multiseptate or contain daughter cysts in a solid matrix. Care must be taken to avoid fluid leakage. According to WHO recommendations, medical pharmacotherapy such as albendozle should be initiated 4 to 30 days prior to surgery and continued for at least 1 month (13).

Finally, public health efforts to prevent transmission of this disease include increasing awareness of exercising good hygiene, such as hand washing before meals, thoroughly cooking food, and wearing protective clothing and gloves when contacting infected fecal material. Also, deworming dogs, controlling the stray population, not feeding raw offal to stray dogs, and enforcing regulated meat inspection procedures by identifying cysts in the intermediate hosts are ways to interrupt the parasite life cycle and thereby mitigate infectivity to humans. Finally, small-scale trials are under way for a recombinant *E. granulosus* vaccine for sheep that may be a promising effort in prevention and control. Additional information on these prevention and control efforts is available through the World Health Organization and the Pan American Health Organization (14, 15).

SELF-ASSESSMENT QUESTIONS

1. How are humans infected with *E. granulosus*?
    a. Ingestion of undercooked lamb
    b. Walking barefoot in areas where sheep graze
    c. Ingestion of food/water contaminated with feces
    d. Ingestion of infected carnivore host
2. What is the most common site of *E. granulosus* cyst development?
    a. Lung
    b. Brain
    c. Liver
    d. Bone
3. Which of the following would not be observed in hydatid sand?
    a. Hooklets
    b. Gravid proglottids
    c. Invaginated protoscolices
    d. Calcerous corpuscles

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